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CATARACT SURGERY – COMPLICATIONS AND TECHNIQUES

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CATARACT SURGERY: COMPLICATIONS AND TECHNIQUES

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ABSTRACT

Cataract surgery is one of the most common surgical procedures performed worldwide. Posterior capsule opacification (PCO) remains the most common postoperative complication that can deteriorate vision. Development of glistenings in the artificial intraocular lens (IOL) after cataract surgery is a phenomenon with the potential to reduce the outcome of an otherwise excellent final surgical result. Phacoemulsification has been the most common surgical technique performed to remove cataracts during the previous 25 years. The settings controlling the fluidics in the eye intraoperatively can affect the postoperative convalescence.

Since many people undergo cataract surgery annually and all of the previously mentioned issues can affect the final outcome, a better understanding and more studies comparing different IOLs and phacoemulsification settings will help surgeons choose better IOLs and surgical techniques and decrease postoperative complications.

In study I, we compared the development of PCO and glistenings associated with two hydrophobic acrylic IOLs, the Sensar AR40e (Abbott Medical Optics) and AcrySof SA60AT (Alcon), 5 to 7 years after cataract surgery. Both IOLs had a sharp posterior edge design. We also evaluated if there were correlations between the amount of glistenings and corrected distance visual acuity (CDVA) or contrast sensitivity and if subjective gradings of glistenings were correlated with the objective quantification of glistenings with Scheimpflug images. Eighty patients were included in this prospective randomized study. Fifty-six patients completed the follow-up visit from 5 to 7 years postoperatively. Glistenings were graded at the slit-lamp microscope and the amount of glistenings was quantified objectively using Scheimpflug images with subsequent processing in computer software. There were no significant differences in PCO area and severity or neodymium:yttrium-aluminium-garnet (Nd:YAG) capsulotomy rates between the IOLs. Significantly more glistenings were found in the AcrySof hydrophobic IOLs 5 to 7 years postoperatively. The glistenings were not correlated with the CDVA or contrast sensitivity.

In study II, we evaluated in a prospective randomized trial if there were any correlations between the amount of glistenings and CDVA or contrast sensitivity and compared the development of glistenings in two acrylic IOLs, a hydrophilic IOL (BL27, Bausch & Lomb) and a hydrophobic IOL (AcrySof SA60AT), 9 years after cataract surgery. One hundred and twenty patients were recruited, 78 completed the 9-year follow-up visit.

The amount of glistenings was quantified objectively using Scheimpflug images with subsequent processing in computer software. Glistenings were also subjectively graded at the slit-lamp microscope. The hydrophobic IOL had significantly more glistenings at the 9-year follow-up visit. The glistenings were not correlated with the CDVA or contrast sensitivity.

In study III, we compared the PCO area, severity, and survival time without Nd:YAG capsulotomy between a hydrophilic (BL27) and a hydrophobic (AcrySof SA60AT) acrylic IOLs 9 years after cataract surgery. One hundred and twenty patients were recruited, 78 completed the 9-year follow-up visit. The PCO area and severity were higher in the hydrophilic IOL. The survival time without Nd:YAG capsulotomy was longer in the hydrophobic IOL.

In study IV, we compared low and standard fluidics settings during phacoemulsification cataract surgery and evaluated the impact on the eye postoperatively by measuring parameters indicating surgical trauma. Forty-three patients were recruited and randomized into two groups, i.e., those that underwent phacoemulsification with low or standard fluidics settings. The central corneal thickness, macular thickness, and intraocular pressure were measured preoperatively, 1 day, 3 weeks, and 3 months postoperatively. The CDVA was measured preoperatively, 3 weeks and 3 months after surgery. Anterior chamber flare was measured preoperatively, 1 day and 3 weeks postoperatively. Endothelial cell density was measured preoperatively and 3 months postoperatively. The low-settings group had a significantly longer surgical time and higher amount of ultrasound energy used intraoperatively, but there were no significant differences in the outcome parameters between the two groups.

In conclusion, significantly more glistenings developed in the AcrySof hydrophobic IOLs 5 to 7 years postoperatively compared to the hydrophobic Sensar IOL. The glistenings were not correlated with the CDVA or contrast sensitivity. The hydrophobic AcrySof IOL developed significantly more glistenings at the 9-year follow-up visit compared to the hydrophilic BL27 IOL. The glistenings were not correlated with the CDVA or contrast sensitivity. The PCO area and severity were higher in the hydrophilic IOL. The survival time without Nd:YAG capsulotomy was longer in the hydrophobic IOL. Phacoemulsification surgery with low fluidic settings rendered significantly longer surgical time and higher amount of ultrasound energy used intraoperatively, but there were no significant differences in the outcome parameters between the two groups.

LIST OF PUBLICATIONS

I. **Chang A, Behndig A, Rønbeck M, Kugelberg M**

Comparison of posterior capsule opacification and glistenings with 2 hydrophobic acrylic intraocular lenses: 5- to 7-year follow-up. ***Journal of Cataract and Refractive Surgery*** **2013 May;39(5):694-698**

II. **Chang A, Kugelberg M**

Glistenings 9 years after phacoemulsification in hydrophobic and hydrophilic acrylic intraocular lenses. ***Journal of Cataract and Refractive Surgery*** **2015 Jun;41(6):1199-1204**

III. **Chang A, Kugelberg M**

Posterior capsule opacification 9 years after phacoemulcification with the hydrophobic AcrySof SA60AT and hydrophilic BL27 intraocular lenses. Submitted 2015-10-01

IV. **Chang A, Fridberg A, Kugelberg M**

Comparison of phacoemulsification cataract surgery with low versus standard fluidic settings and the impact on postoperative parameters. Submitted 2015-09-01

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LIST OF ABBREVIATIONS

BSS	Balanced saline solution
CCT	Central corneal thickness or computer compatible tape
CDE	Cumulative dissipated energy
CDVA	Corrected distance visual acuity
CME	Cystoid macular edema
ECD	Endothelial cell density
IOL	Intraocular lens
IOP	Intraocular pressure
Nd:YAG	Neodymium:yttrium-aluminium-garnet
OCT	Optical coherence tomography
PMMA	Polymethyl methacrylate
PCO	Posterior capsule opacification
POCOman	Posterior capsule opacification software

1 LENS GLISTENINGS

1.1 INTRODUCTION

Glistenings were first reported in polymethyl methacrylate (PMMA) intraocular lenses (IOLs)[1]. However, it was after the introduction of the popular hydrophobic acrylic AcrySof IOL (Alcon) in 1994 that glistenings caught the attention of clinical researchers, who then began investigating if this phenomenon had any substantial clinical impact on vision.

1.2 DEFINITION

Glistenings are defined as fluid-filled microvacuoles that form within the IOL when it is in an aqueous environment[2].

1.3 GLISTENING FORMATION, ONSET, AND SIZE

The formation process of lens glistenings remains controversial. Two theories have been proposed. The first theory suggests that formation of microvoids inside the IOL material occurs during the polymerization process in one of the IOL production steps. The microvoids slowly absorb water when the IOL is in the aqueous environment. When water vapor detaches from the surrounding matter inside the microvoids, a reaction called phase separation occurs. Because there are differences in the refractive indices between water and the surrounding IOL material, light scatters when it passes between the two media and appears as sparkling dots, hence, the term glistenings[2].

The water absorption rate differs between different IOLs and the surrounding environment regarding temperature[3] and osmotic level[4]. Different IOLs have different glass transition temperatures (Tgs). When the temperature is above the Tg, the IOL absorbs water faster and is soft and flexible. Below the Tg, the IOL is rigid and the water absorption rate is slower. Hydrophobic acrylic IOLs have Tgs close to room temperature, 20 Cº for the hydrophobic AcrySof IOL. A temperature below 15°C has not been associated with glistening formation in the most commonly implanted IOLs[5].

In vitro experiments in which IOLs were exposed to temperature variations, mimicking accelerated glistening formation that could take years in vivo, showed that when the IOLs are suspended in an aqueous environment and heated, the IOLs become oversaturated with water. However, after cooling, causing phase separation in the microvoids of the IOLs, glistenings are observed because of the difference in the refractive indices between water and the surrounding IOL material as mentioned previously.

The second theory suggests that as hydrophilic impurities enter the microvoids inside the IOL material, the osmotic gradient inside the voids increases from the surrounding aqueous environment, causing an influx of water through diffusion with subsequent expansion of the microvoids. When a critical level of expansion is reached, probably causing cracks and tears in the IOL material surrounding the microvoids, they become permanent[4]. Repeated heating and cooling of the IOL showed that glistenings appear at the same locations in the IOL[6].

Glistenings can develop as soon as 1 week after cataract surgery[7] in sizes ranging from 1 to 20 microns[6 8-10], often 1 to 10 microns in clinical cases. In vitro studies with more extreme environmental variations can generate glistenings with sizes up to 20 micron or larger.

1.4 FACTORS AFFECTING GLISTENING FORMATION

Different IOL materials, hydrophilic, hydrophobic, PMMA, and silicone IOLs have been identified to develop glistenings to different degrees[7 11-13]. Time is also crucial; the longer time that has passed since IOL implantation the more likely it is that glistenings will develop or the number of existing glistenings will increase[13-16].

The IOL dioptric power[17], IOL packaging[18], IOL manufacturing technique[19], temperature changes[6], glaucoma[20], uveitis and other conditions with breakdown of the blood-aqueous barrier[21], use of antiglaucoma eye drops,[20 22] and anti-inflammatory eye drops containing surfactant may have a role in glistenings formation[23 24].

When the AcrySof hydrophobic acrylic IOL was introduced to the market in 1994, it was delivered packed in the AcryPak system, containing both the IOL and a folder in a plastic case that was sterilized in the plastic case. One of the first reports of glistenings in AcrySof IOLs was associated with this IOL packaging system. The increased glistenings in the IOLs in the AcryPak compared to the same IOLs in the so-called Wagon Wheel packages led to the conclusion that the microenvironment in the AcryPak system was changed and hence the development of glistenings increased[18].

The production of IOLs is divided into two principal techniques: cast molding and lathe-cutting. The former is suitable for large quantity production and involves polymerization of IOL monomer mixtures in casting molds. Parts of heterogeneous unreacted monomers can still be present in the molds and may explain why in some studies there are more glistenings in IOLs produced with cast molding compared to lathe-cutting[19].

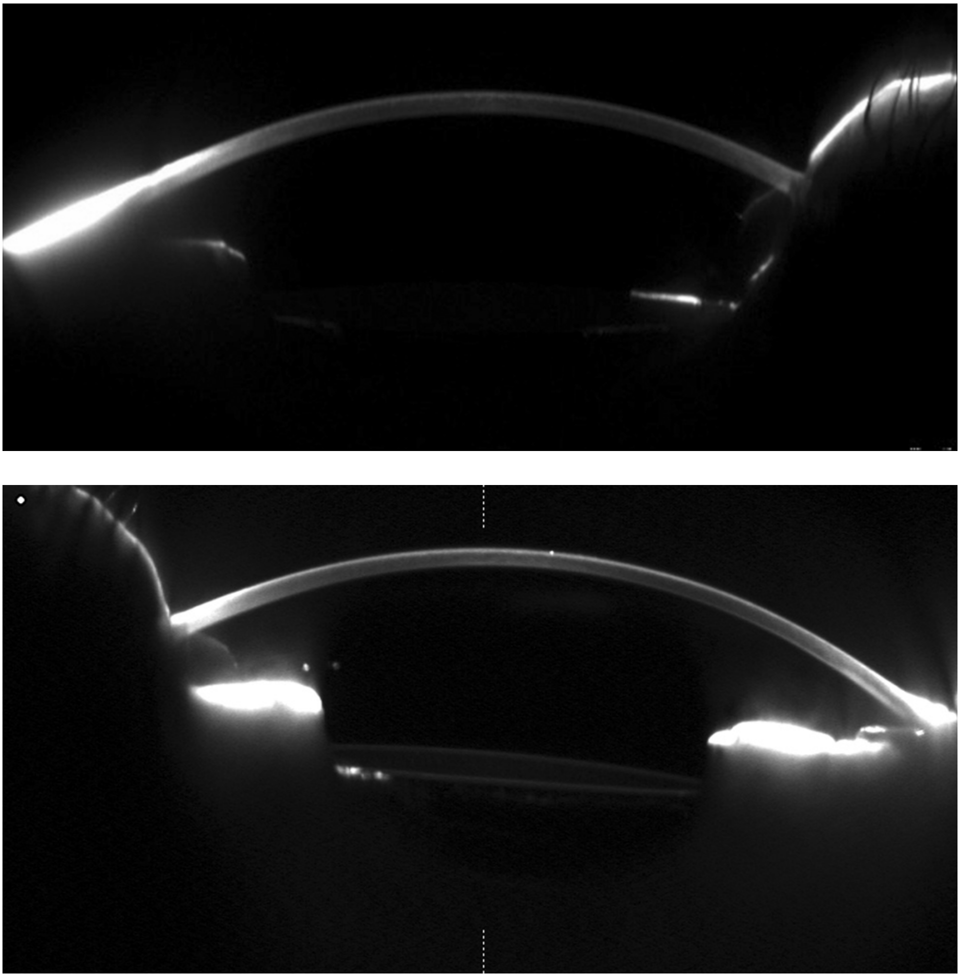
The latter, lathe-cut IOLs, are produced from mixtures of monomers polymerized into large acrylic sheets and IOLs from homogenous parts of the sheet are subsequently cut out from the sheet and polished.

1.5 METHODS TO ASSESS AND GRADE GLISTENINGS

Glistenings can be graded in two ways. Most commonly subjective grading systems of 0 to 3[25] and 0 to 4 have been used[7 14 26 27], with 0 representing no glistenings, 1 trace, 2 minor, 3 moderate, and 4 severe. The examiner grades the glistenings based on how many glistenings the IOL appears to have under slit-lamp microscopy. To grade glistenings objectively and facilitate quantitative comparisons between studies and reproduction of the results, Professor Behndig invented a method of analyzing glistenings performed with Scheimpflug images[13 14 23 28 29].

The Scheimpflug technique uses the ability to rotate around the visual axis and scan the IOL at different angles, capturing optical sections with the camera's charge-coupled device sensor. When two two-dimensional sections of images perpendicular to each other are used in the subsequent analysis with computer software, they produce a three-dimensional image. The amount of reflected light scattering is measured in computer compatible tape (CCT) with 256 levels of brightness, ranging from 0 for black to 255 for white. Within this three-dimensional image, the CCTs represent glistenings and are calculated with computer software. Images of light scatterings in the IOLs are illustrated in figure 1.

Figure 1. Scheimpflug images show no glistenings in the superior image and glistenings in the entire thickness of the IOL in the inferior image.



Another phenomenon is called surface light scattering[30 31], which should not be confused with glistenings. Surface light scattering is likely caused by water phase separation, surface deposition of a biofilm, or both at the IOL surface-water contact face. Often surface light scattering is visible in the Scheimpflug images as two whitish bands on the anterior and posterior parts of the IOL just beneath the IOL surface.

1.6 PROGRESSION OVER TIME

Several studies, some of which were long term, have reported that glistenings progress over time in all IOLs[7 13], but especially in the hydrophobic acrylic AcrySof IOLs[7 12-15]. However, some studies have reported that glistenings tend to stabilize after a certain time[10 20].

In a study[7] with up to a 2-year follow-up, the earliest glistenings were observed as early as 1 week after cataract surgery and increased thereafter up to 90 days. After 180 days, the amount of glistenings in all IOLs included in the study (2 silicone, 3 hydrophilic acrylic, and 2 hydrophobic acrylic) stabilized; however, in the AcrySof (hydrophobic acrylic) and CeeOn Edge 911A (Pharmacia & Upjohn Co.) (silicone) IOLs, the glistenings continued to increase.

Another study[15] that followed patients up to 50 months postoperatively also confirmed increasing amounts of glistenings with time. Two other studies[21 32] also reported that glistenings increase with time.

In one in vivo study[20] the incidence and severity of glistenings did not increase up to 24 months postoperatively. One in vitro study[10] showed that glistenings stabilizes after a certain time after the IOL was immersed in an aqueous environment.

1.7 GLISTENING IN DIFFERENT IOL MATERIALS

1.7.1 Glistenings in hydrophobic IOLs

Hydrophobic acrylic IOLs, especially AcrySof IOLs, have received most attention in previous studies of glistenings. The AcrySof MA60BM (Alcon), Sensar AR40e (AMO), Acryfold VA-60BB (HOYA), Nex-Acri N4-18B (NiDEK), and Avansee AU (Kowa Co.) were studied in vitro for accelerated glistening formation in a laboratory test simulating 20-year deterioration of acrylic IOLs[12]. All IOLs but the Avansee AU6 developed glistenings.

Two other IOLs, XACT X60 (Advanced Vision Science) and enVista MX60 (Bausch & Lomb), both made of the same material, claimed that no glistenings developed in 2-year and 6-month follow-up studies[33-35].

1.7.2 Glistenings in hydrophilic IOLs

There are few studies on hydrophilic acrylic IOLs and glistenings development. Tognetto et al.[7] evaluated three hydrophilic IOLs: the ACR6D (Corneal Laboratories), Hydroview

(Bausch & Lomb), and Stabibag (Ioltech). The three IOLs developed increased mean grades of glistenings in 23% to 45% of eyes from 7 to 90 days after implantation and remained stable thereafter until the follow-up endpoint at 2 years.

In a simulated 20-year deterioration test of acrylic IOLs[12], the Hydroview HP60M (Bausch & Lomb) IOL did not show any opacities.

Hydrophilic IOLs tend to not develop glistenings as much as IOLs made of other materials. One possible reason is that they contain higher amounts of water. Water content in hydrophilic IOLs is often more than 18%. In hydrophobic IOLs, the water content is usually lower than 1%. A new hydrophobic IOL, the enVista contains 4% water. The manufacturer claims that the enVista IOL was glistenings-free in a 6-month follow-up study[33]. If it is still glistening-free over the longer run, then it would be interesting to discuss if the water content in hydrophilic IOLs is the main reason for the low incidence and amount of glistenings.

1.7.3 Glistenings in PMMA IOLs

The first report of glistenings in IOLs in 1984 was based on a PMMA IOL. In a study of the progression of glistenings by Wilkins and Olson[32], no glistenings were observed the first 3 years in the Surgidev B20/20 IOL (Surgidev Corporations). After 7 years all IOLs had developed glistenings. The frequency and size of glistenings increased with increased follow-up time.

Rønbeck et al.[13] compared the development of glistenings 12 years postoperatively in PMMA, silicone, and hydrophobic acrylic AcrySof IOLs. The study showed almost no glistenings in the PMMA IOL, and the amount of glistenings was significantly higher in silicone and hydrophobic IOLs than in the PMMA IOL.

1.7.4 Glistenings in silicone IOLs

Tognetto et al.[7] studied two silicone IOLs, the CeeOn Edge 911A (Pharmacia & Upjohn Co.) and the SI-40NB (AMO). Glistenings increased up to 90 days in the SI-40NB IOLs and then stabilized. However, the CeeOn® Edge 911A IOL had a continuous increase in the mean grade of glistenings at the endpoint of the study 2 years postoperatively. Rønbeck et al.[13] found that the silicone IOL (SI-40NB) developed more glistenings than the PMMA IOL but less than the hydrophobic AcrySof IOL 12 years postoperatively.

1.8 EFFECT ON VA AND CONTRAST SENSITIVITY

It seems logical that glistening should adversely affect the CDVA and contrast sensitivity because the tiny microvacuoles in the IOL scatter the light passing through the IOL and therefore cause deteriorated CDVA or glare. However, no studies up to now support any significant correlations between diminished CDVA and glistenings.

For the examiner, it is obvious when performing neodymium:yttrium-aluminium-garnet (Nd:YAG) capsulotomy in a patient with an IOL with severe glistenings, that it is more difficult to target the laser beam at the posterior lens capsule in the Nd:YAG slit-lamp.

It remains controversial if glistenings affect contrast sensitivity. Most studies have not reported any correlation[20 28 36 37]. However, some studies have shown that contrast sensitivity is affected[25] and some only at high spatial frequencies[27 38].

2 POSTERIOR CAPSULE OPACIFICATION

2.1 INTRODUCTION

Posterior capsule opacification (PCO) is the most common complication after phacoemulsification cataract surgery. The incidence rates range from less than 10% to 50%[39-41]. PCO was observed in the early days of IOL implantation at the end of the 1940s. With a successively better understanding of the pathogenesis and treatment options for PCO, we can now with modern cataract surgery gradually decrease the incidence of PCO with the help of better tools[39], such as continuous development of safer phacoemulsification machines facilitating more thorough cortical removal of lens material, better IOL materials and designs that inhibit PCO, and even surgical laser systems to create customized repeatable and perfect capsulorhexis sizes, avoiding the unnecessary risk of making too large or off-center capsulorhexes and hence decreasing the risk of PCO development[42-44].

Studies have been done with immunotherapy, gene therapy, chemical therapy, and physical techniques to eliminate lens epithelial cells (LECs)[45-47].

PCO is still far from eradicated. The only treatment is outpatient Nd:YAG laser capsulotomy for cooperative patients. However, because of the total number of cataract surgeries annually, it is a societal economic burden[48] and Nd:YAG lasers are not readily available everywhere, especially in rural areas in developing parts of the world. For the patient, Nd:YAG capsulotomy is associated with several sight-threatening complications such as retinal detachment[49 50], macular edema[51], intraocular inflammation[50], transient increased intraocular pressure (IOP)[51 52], increased vitreous opacities[53], IOL damage[50 54] and IOL dislocation[55].

PCO causes symptoms when light passes through the opacified posterior lens capsule and is forward-scattered to the retinal fundus. Symptoms such as decreased VA and contrast sensitivity, increased glare, diplopia, and blurred images are typical[56 57]. The symptoms may cause disabilities in daily life, for example, when driving a car and especially when driving at night. The amount and density of PCO may not be experienced or expressed similarly regarding severity by different patients[58]. The CDVA also can be better or worse than expected compared to the PCO status observed by the physician.

2.2 PATHOPHYSIOLOGY

Phacoemulsification cataract surgery removes the opacified lens nucleus and cortex. Two types of remnant LECs proliferate and migrate from the equatorial zone of the anterior lens capsule (A-cells) or equatorial lens bow (E-cells) toward the central optical zone with time[48]. When LECs are in the central parts of the posterior lens capsule, they scatter light entering the posterior segment of the eye causing deteriorated CDVA, glare, and distorted images. A-cells transformed into myofibroblasts cause fibrosis and shrinking of the anterior lens capsule and may lead to IOL tilting and decentration. E-cells have a high capacity for mitosis and differentiation into balloon-like bladder cells (Wedl cells) and can form Elschnig's pearls, a regenerative form of lens capsule opacification and the most common PCO, characterized clinically as having a pearl-like appearance. A special form of regenerative PCO is Soemmerring's ring, a doughnut-shaped opacity described as early as 1828 with formation of Elschnig's pearls retained at the periphery of the anterior-posterior capsule fuse as a ring-shaped lesion[59].

2.3 FACTORS AFFECTING PCO

Earlier studies have suggested that age[60], uveitis, diabetes mellitus[61-65], retinitis pigmentosa[66], surgery techniques[43 44 67], IOL material[68-72], and IOL design[53 73-77] are PCO-related factors.

The sharp-edge design of IOLs is probably the most important factor inhibiting PCO development[74]. In a comparative study between two single-piece hydrophilic acrylic IOLs[78], one IOL was a standard model with a sharp posterior edge except at the optic-haptic junctions. The other IOL had an enhanced edge with a peripheral ridge around the lens optic 360º circumferentially. The latter developed significantly less PCO than the standard model.

Round-edge IOLs were shown in previous studies to be inferior to sharp-edge IOLs in inhibiting PCO[74 78-84]. The sharp posterior IOL edge acts as a barrier by bending in the posterior lens capsule against the sharp posterior square-edge IOL and thus inhibiting migration of LECs from the equator of the lens capsule to the central parts of the IOL optic[75 77].

Nishi et al.[74] compared development of PCO between a round-edge and a sharp-edge AcrySof IOL and reported that the round-edge IOL developed significantly more PCO. The authors concluded that the sharp-edge IOL design was the main PCO inhibitory factor and the IOL material instead has a complimentary role in inhibiting PCO development[74]. Angulation of the IOL haptics enhances the force exerted on the bending between the posterior lens capsule and the sharp IOL edge and increases the integrity of the barrier[85]. However, the sharpness of the square-edge IOL can vary between IOLs of different materials[81] or even the same materials[86]. Generally, most hydrophilic IOLs have rounder edges than hydrophobic IOLs probably because during the manufacturing process hydrophilic IOLs are lathe-cut from dehydrated IOL blocks and then polished leading to loss of the sharp edge[81]. However, hydrophilic IOLs with sharp edges also exist.

Comparisons of IOL materials have shown that hydrophilic IOLs develop PCO at higher rates than hydrophobic IOLs, 50.3% in a hydrophilic IOL compared with 4.9% in a hydrophobic IOL in a 1-year follow-up study by Heatley et al[68]. Other studies with 1- to 3-year follow-ups also have reported similar results[69 87 88]. Linnola et al.[89 90] argued that fibronectin bindings between the posterior lens capsule and the IOL surface of hydrophobic acrylic IOLs seem to have an important role in inhibiting migration of LECs by increasing the barrier effect. However, in studies with more than 3 years of follow-up postoperatively that compared hydrophobic acrylic with silicone and PMMA IOLs, the PCO incidence and Nd:YAG capsulotomy rates increase in the hydrophobic IOLs are equal to or even surpass the rates for silicone IOLs[91-93]. One theory is that the barrier effect of the sharp posterior edge design in acrylic IOLs that inhibit PCO development gradually may be compromised when increasing amounts of slowly migrating LECs physically force the reopening of the barrier between the IOL edge and posterior lens capsule[91 92].

2.4 METHODS TO ASSESS PCO

Most earlier studies have analyzed PCO with retroillumination images. Several image computer software packages are available with their respective advantages and disadvantages. Evaluation of Posterior Capsule Opacification software (Augentagesklinik Spreebogen) evaluates PCO subjectively. Posterior Capsule Opacification software (POCOman, Kings College) evaluates PCO semiobjectively, Posterior Capsule Opacification software and Automated Quantification of After-Cataract (Medical University of Vienna) processes the PCO images in the computer software to calculate the size of the area at the posterior capsule that is affected by PCO and determine the PCO density[94-96].

Nd:YAG laser capsulotomy frequency is considered another important parameter for evaluating PCO. This parameter correlates well with the CDVA but has a weaker correlation with the contrast sensitivity[97]. Scheimpflug images have also been used in PCO studies[98].

Patients who already underwent Nd:YAG capsulotomy cannot be evaluated by any of the above-mentioned computer software since there is no posterior capsule. This problem was addressed previously[99]. These patients received the highest scores for PCO area and severity in studies I and III. We assumed if they have not had Nd:YAG capsulotomy earlier they would have had a high grade of PCO.

Long-term studies also have an increased number of patient dropouts with increased follow-up time. Patients get older, some die, and some get ill during the follow-ups. Information about Nd:YAG capsulotomy frequency becomes uncertain when this information only comes from patients living long enough or those healthy enough to complete the follow-up examination. It is possible that some dropouts would have had Nd:YAG capsulotomy at the follow-up visit if they had arrived for the examination. However, the capsulotomy data are only obtained from patients at the follow-up visits. To collect as much information as possible from all patients, we used survival analysis, which has been used in earlier similar studies[13 99]. The analysis has the advantage of considering the data from patients until they are lost to follow-up.

2.5 PROGRESSION OVER TIME

PCO frequency has been reported with great variability from 10% to 60% in different studies. Since the introduction of IOLs with a sharp posterior edge profile, the PCO frequency can be as low as about 10% 5 years postoperatively[39 40].

Development of PCO in different IOL materials shows different patterns. Two follow-up studies[100 101] have reported that the Nd:YAG capsulotomy rates increased from the 2-year to the 5-year follow-up for three different IOLs, a PMMA, a silicone, and a hydrophobic acrylic. The Nd:YAG rate increased from 20% to 61% for the PMMA (HSM 809C) IOL (Pharmacia & Upjohn), 22% to 33% for the silicone (SI-40NB) IOL, and 8% to 22% for the hydrophobic acrylic (AcrySof MA60BM) IOL.

3 FLUIDICS IN PHACOEMULSIFICATION

3.1 INTRODUCTION

Modern cataract surgery is performed using the phacoemulsification technique[102 103]. This technique has the advantages of small incision wounds, faster sight rehabilitation, less damage to the intraocular tissues, and minimal intraoperative and postoperative complications compared to previous surgical techniques[104-107].

To extract the opacified lens with a diameter of about 10 millimeters through a 2- to 3-millimeter incision, the lens is divided into smaller fragments. This is done with the phacoemulsification tip inserted through the incisional wound to divide the lens into smaller fragments and aspirate the lens fragments through the tip opening. The tip uses ultrasound energy to emulsify the lens, builds up heat in and around the tip, and can damage the surrounding tissues. The tip also has two other functions, i.e., irrigation and aspiration. Irrigation helps cool the heat around the tip by producing an inflow of saline solution that dilutes the heat near the tip. Aspiration also maintains stabilized fluid volume in the anterior chamber and drains excess heat from the eye. Lens fragments follow the irrigating fluid flow to the opening of the tip. When lens material fully occludes the tip opening, the machine then uses vacuum to crush and suck (i.e., aspirate) the material into a waste bag in the machine through the hand-piece connected to the tip. Modifying the irrigation and aspiration settings in the phacoemulsification machine can create different effects to enhance and facilitate a smooth surgical procedure. The surgeon may ensure a surgery with a stable anterior chamber and good followability by changing the settings for different anatomic variations in eyes or different hardnesses of the lens nucleus. Most surgeons have their own settings during the different surgical phases: sculpting, lens consumption and removal of remaining lens cortex. However, some questions remain unanswered. Some surgeons claim that minimizing fluid turbulence intraoperatively may cause less surgical trauma to the eye compared to the standard settings most surgeons use. However, few studies have been conducted in this field[108 109].

3.2 PARAMETERS INDICATING SURGICAL TRAUMA

We know from earlier studies that a large amount of ultrasound energy is dissipated from the phacoemulsification tip and increases the possibility of a cornea with more swelling[110], anterior chamber reaction[111-114], cystoid macular edema (CME)[115 116], increased postoperative IOP, and decreased corneal endothelial cell density (ECD)[108].

3.3 METHODS TO MEASURE THE PARAMETERS INDICATING SURGICAL TRAUMA IN PHACOEMULSIFICATION

The central corneal thickness (CCT) can be measured by different pachymetric methods[117-119]. Most often optical or ultrasound diagnostic tools are used. The examiner can visually detect CME, but posterior-segment optical coherence tomography (OCT) can be performed to quantify and compare the results[120]. ECD measurements can be obtained with confocal microscopy[121]. An anterior chamber reaction can be detected and quantified with a flare meter[111 122 123].

3.4 EFFECT ON VISION

Increased CCT, CME, anterior chamber reaction, high IOP, and decreased ECD are all factors that can solely or in combination cause diminished CDVA.

4 GENERAL AIMS

In study I, our goal was to determine if two hydrophobic acrylic IOLs develop PCO and glistenings differently and if glistenings affected VA and contrast sensitivity 5 to 7 years after phacoemulsification cataract surgery.

In study II, we evaluated a hydrophobic and a hydrophilic acrylic IOL and compared the development of glistenings and the impact on VA and contrast sensitivity in the IOLs 9 years after phacoemulsification cataract surgery.

In study III, we evaluated the same hydrophobic and hydrophilic acrylic IOLs as in study II and compared the development of PCO and survival without Nd:YAG capsulotomy in the IOLs 9 years after phacoemulsification cataract surgery.

In study IV, we compared two different fluidic settings in phacoemulsification cataract surgery and the impact on postoperative parameters.

5 MATERIALS AND METHODS

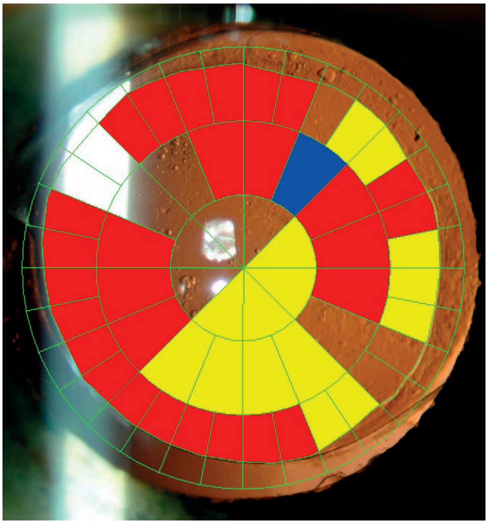
5.1 STUDY I

5.1.1 Study design

The 80 patients who underwent cataract surgery from 2002 to 2005 in this prospective study were randomized into two equal groups of 40 patients each. One group received the three-piece Sensar AR40e IOL and the other group received the one-piece AcrySof SA60AT IOL; both IOLs are made of a hydrophobic acrylic material with a sharp posterior IOL edge design. The patients were contacted for a follow-up visit during 2010. The CDVA measurements obtained with the 100% and 2.5% Early Treatment Diabetic Retinopathy Study (ETDRS) charts were recorded in the logarithm of the minimum angle of resolution scale. We obtained retroillumination images of PCO with a fundus camera and Scheimpflug images of glistenings with the Pentacam HR (OCULUS Inc.).

The retroillumination images of PCO were loaded into a posterior capsule opacity computer software system (POCOman) and calculated semiobjectively, because some steps in the analysis required manual interactions. The program applied a grid pattern on the retroillumination images and divided the area into 56 approximately equal sectors. The area outside the capsulorhexis was excluded from analysis. The examiner marked any sector with PCO covering more than 50% of the area and graded the severity of PCO as 0 indicating no PCO, 1 mild, 2 moderate, and 3 severe. The software then calculated the overall severity of the PCO ranging from 0 to 3 and the total area of the PCO as a fraction of the affected area divided by the total area within the capsulorhexis (figure 2).

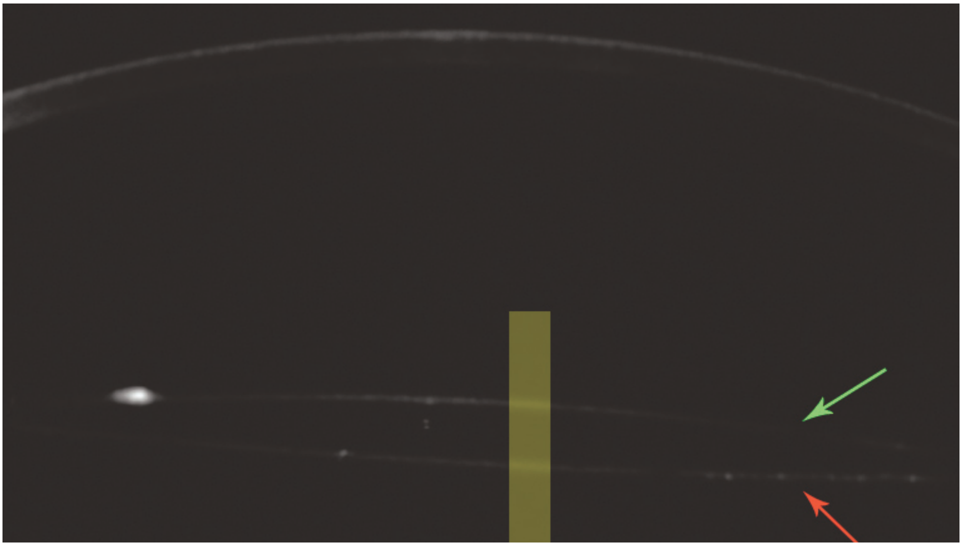
Figure 2. POCOman software quantifies PCO area and severity.



The examiner scores the severity of PCO for any sector with more than 50% of the area affected by PCO using color codes. No markings indicate 0, blue 1, yellow 2, and red 3.

Quantitative glistening analysis was conducted objectively by loading two Scheimpflug images, a superior and a temporal camera position, of the IOL into ImageJ image analysis software (National Institute of Health). A small rectangular box comprised of the entire IOL thickness and including the area anterior and posterior to the IOL within the central 1.5 millimeters zone of the visual axis was selected for analysis (figure 3). The raw data extracted from the software were subsequently imported into a macro in Excel software (Microsoft Corp.) to perform the calculations. The macro was written to calculate the light scattering in the IOL and calibrate it against the minute light scattering in the aqueous humor. The peak light scattering in the posterior part of the IOL was interpreted as the posterior lens capsule and not included in the calculations. The output result was the amount of glistenings in arbitrary units.

Figure 3. Selecting the area of interest in glistening analysis. The yellow box, placed within the central 1.5 mm zone of visual axis, is the area selected for glistening analysis. The green arrow indicates the anterior IOL surface; the red arrow indicates the posterior IOL surface.



We analyzed glistenings in three ways: the full IOL thickness, as deep glistenings by subtracting the light scattering in the Scheimpflug images in the 73 microns of the most anterior part and the 73 microns of the most posterior part of the IOL from the total amount of the light scattering in the full IOL thickness, and as very deep glistenings by subtracting the light scattering in the 103 microns of the most anterior part and the 103 microns in the most posterior part of the IOL from the total amount of light scattering in the full IOL thickness. The calculations with the two last-mentioned ways omitted the light scattering from the anterior and posterior IOL surfaces, which omits surface light scattering from the calculations.

Subjective gradings of the glistenings at the slit-lamp microscope were recorded according to a grading system with scoring from 0 to 3, with 0 indicating no glistening, 1 trace, 2 moderate, and 3 severe.

5.1.2 Inclusion and exclusion criteria

Patients 39 to 86 years old with cataracts were included. Patients were excluded who had moderate or advanced age-related macular degeneration, corneal pathology, earlier retinal photocoagulation, diabetes mellitus, glaucoma, exfoliation syndrome, and uveitis, and those who received preoperative oral steroid therapy or underwent a previous intraocular surgery.

5.1.3 Surgery

One experienced surgeon performed the cataract surgery using phacoemulsification with a clear corneal incision. The surgical procedure was initiated with topical and intracameral anesthesia. Sodium hyaluronate was used as an ophthalmic viscosurgical device (OVD). Continuous capsulorhexis was followed by hydrodissection with balanced saline solution (BSS) and phacoemulsification in the capsular bag. Irrigation and aspiration of the remaining cortex were performed and one of the two IOLs was folded and injected into the capsular bag. The procedure ended with an intracameral injection of cephalosporin as antibiotic prophylaxis, and the corneal wound was hydrated with BSS using a blunt injection needle. The patients instilled topical dexamethasone in a tapering dose during the first 3 postoperative weeks.

5.1.4 Statistical analysis

Quantitative comparisons of the PCO area and severity and the amount of glistenings were analyzed with the Mann-Whitney U-test. Nd:YAG capsulotomy rates to compare the two IOLs were calculated using Fisher’s exact two-tailed test. All calculations for correlations were conducted with the Spearman rank-order correlation.

5.2 STUDY II

5.2.1 Study design

This was a prospective randomized study that included 120 patients, who had phacoemulsification cataract surgery between 2002 and 2004. The patients were randomized to one of two groups and received either the hydrophilic BL27 IOL or the hydrophobic AcrySof SA60AT IOL, both of which were one-piece acrylic IOLs with sharp posterior edges. Nine year after surgery the patients were contacted for a follow-up examination.

Lens glistening analysis was conducted in the same way as in study I with Scheimpflug images with subsequent data processing using computer software for objective quantification and grading at the slit-lamp for subjective scoring.

The CDVA and contrast sensitivity were measured using the Optec® 6500 Vision Tester (Stereo Optical Co., Inc.), with an ETDRS chart for the CDVA measurements and Functional Acuity Contrast Test (F.A.C.T, Stereo Optical Co., Inc.) for the contrast sensitivity measurements. The F.A.C.T is a sine-wave grating chart that tests the functional VA in five spatial frequencies (1.5, 3, 6, 12, and 18 cycles per degree) and nine levels of contrast. The patient determined the minimal contrast grating level seen for each spatial frequency. The last correct grating level identified for each spatial frequency was plotted on a contrast sensitivity curve. The area under the curve value was used in the statistical analysis to determine any correlation with the amount of glistenings. This method of measuring the contrast sensitivity is more accurate than other available contrast sensitivity measurements[124]. The contrast sensitivity measurements were conducted with and without glare. When testing with glare, 12 light-emitting diode lamps were arranged in an oval arc around the testing field and lighted.

5.2.2 Inclusion and exclusion criteria

Patients 60 to 90 years old with senile cataracts were included. Patients were excluded who had a dilated pupil less than 6 millimeters; a previous history of intraocular surgery, corneal endothelial damage, or ocular trauma; traumatic cataract; pseudoexfoliation syndrome; uveitis; diabetic retinopathy; glaucoma; or advanced macular degeneration; and those receiving long-term anti-inflammatory treatment.

5.2.3 Surgery

One of three experienced surgeons performed the phacoemulsification surgeries. The surgical procedures were the same as described for study I.

5.2.4 Statistical analysis

The follow-up time between the two IOLs was compared using the Student’s t-test. The comparison of the amount of glistenings associated with the two IOLs was calculated with the Wilcoxon rank-sum test. The correlations between glistenings, CDVA, and contrast sensitivity were analyzed using the Spearman rank-order correlations.

5.3 STUDY III

5.3.1 Study design

The study design was the same as described for study II.

The PCO area and severity analyses were conducted with POCOman software in the same way as in study I. The survival time without Nd:YAG laser capsulotomy was recorded and defined as the time from the date of surgery to that of Nd:YAG laser capsulotomy.

5.3.2 Inclusion and exclusion criteria

The inclusion and exclusion criteria were the same as in study II.

5.3.3 Surgery

The surgical procedures were the same as described for study II.

5.3.4 Statistical analysis

The comparisons of the follow-up time and average age at surgery between the two groups were calculated with the Student's t-test. The Mann-Whitney U-test was used to compare the PCO area and severity. The Gehan-Wilcoxon test and log-rank test were used to calculate the survival rate without Nd:YAG capsulotomy.

5.4 STUDY IV

5.4.1 Study design

This prospective randomized study included 43 patients who underwent phacoemulsification cataract surgery from 2012 to 2015 at St. Erik Eye Hospital. Patients were randomized to torsional phacoemulsification performed using the Infiniti Vision System (Alcon Inc.); the stop-and-chop technique was used with either low or standard fluidic settings. The low-settings group had the bottle height and aspiration parameters of the phacoemulsification machine at about half the standard settings and vacuum at 73% of the standard settings, which diminishes the fluid turbulence in the anterior chamber and the IOP levels intraoperatively. The amount of saline used intraoperatively, the duration of surgery, and the cumulative dissipated energy (CDE) were recorded. The parameters indicating surgically induced trauma were measured preoperatively as reference values and compared with the values at the postoperative follow-up visits on 1 day, 3 weeks, and 3 months postoperatively. The measurements included the CDVA tested with the ETDRS chart, IOP measured by Goldmann applanation tonometry, macular thickness measured on posterior-segment OCT images, CCT measured on anterior-segment OCT images, ECD using confocal microscopy, and anterior chamber flare using a laser flare meter.

5.4.2 Inclusion and exclusion criteria

Patients 50 to 85 years old with cataracts were included. The exclusion criteria were the same as in studies I-III with addition of traumatic, extremely dense cataract or subluxated lenses; an anterior depth shallower than 2.1 millimeters, pupillary dilation with cyclopentolate-phenylephrine less than 5 millimeters, previous retinal photocoagulation, ECD less than 1,500 cells/mm^2 and medical treatment with corticosteroids or non-steroidal anti-inflammatory drugs.

5.4.3 Surgery

One cataract surgeon performed standard torsional phacoemulsification using the Infiniti Vision System. The procedure began with creation of a clear corneal incision, followed by administration of intracameral anesthesia and a cohesive OVD (1.5% sodium hyaluronate, Z-HYALIN plus, Carl Zeiss Medical AG). A continuous capsulorhexis and subsequent hydrodissection with BSS and phacoemulsification in the capsular bag and irrigation and aspiration of the remaining lens cortex with BSS using an instrument tip were performed. An acrylic hydrophobic IOL, the AcrySof IQ SN60WF, was folded and injected into the capsular bag followed by OVD removal. The corneal wound was hydrated with BSS using a blunt injection needle. The procedure ended with an intracameral injection of moxifloxacin as antibiotic prophylaxis. The patients instilled topical dexamethasone three times daily in a tapering dose during the first 3 postoperative weeks.

5.4.4 Statistical analysis

Normally distributed data were analyzed with the Student’s t-test to compare the groups and the paired t-test to compare within the groups. Non-parametric data analysis was conducted with the Wilcoxon rank-sum test to compare two groups, and the postoperative differences were compared to the preoperative values within the group with repeated measure analysis of variance (Friedman) and the Wilcoxon signed-rank test.

The means and SDs in parametric data and medians with lower and upper quartiles for the measured non-parametric data were calculated for both groups.

6 RESULTS

6.1 STUDY I

6.1.1 Patient data

The study included 80 patients divided evenly between two groups. Fifty-six patients completed a follow-up visit between 5 to 7 years after phacoemulsification cataract surgery. The average age of the patients at surgery was 68.2 years ± 9.7 (SD) (range, 39-86 years).

6.1.2 PCO and Nd:YAG capsulotomy

There were no significant ($P>0.05$ for all comparisons) differences between the groups in PCO area and severity or Nd:YAG capsulotomy.

6.1.3 Glistenings

The AcrySof SA60AT IOL developed significantly more glistenings detected by quantitative Scheimpflug image analysis compared to the Sensar AR40e IOL not only when the full thickness of the IOL was analyzed but also when deep glistenings and very deep glistenings were compared between the two IOLs ($P<0.001$ for all 3 comparisons) . Similar results were also observed when obtaining the data based on the subjective gradings of glistenings at the slit-lamp microscope. No glistenings were seen in 24 of 27 IOLs and mild glistenings in the remaining three IOLs in the Sensar AR40e IOL group. The AcrySof IOL was characterized by even distribution of glistening severity, but more of these IOLs had mild glistenings. The quantitative analysis of glistenings using Scheimpflug images was correlated with the subjective gradings of glistenings ($R=0.61$; $P<0.05$). The IOL power, contrast sensitivity, or CDVA were not correlated with the amount of glistenings ($R=0.13$, $P>0.05$; $R=0.16$, $P>0.05$; and $R=0.1$, $P>0.05$, respectively).

6.2 STUDIES II AND III

6.2.1 Patient data

Study II included 120 patients divided evenly into two groups. The mean patient age was 72.8 years ± 6.7 years (SD) (range, 60-84 years) at surgery. At the 9-year follow-up visit, 78 patients, 42 in the hydrophilic BL27 group and 36 in the hydrophobic AcrySof SA60AT group, completed the examination.

6.2.2 Glistenings

The hydrophobic AcrySof SA60AT IOL developed a significantly higher amount of glistenings compared to almost no glistenings in the hydrophilic BL27 IOL based on quantitative analysis in 3 different IOL depths (full thickness, deep glistenings and very deep glistenings) with Scheimpflug images ($P<0.001$, for all 3 comparisons). Subjective grading of glistenings by slit-lamp microscopy showed evenly distributed severity scores of 0 to 3 (0 indicates no glistenings, 1 trace, 2 moderate, 3 severe) in the hydrophobic AcrySof SA60AT IOL and only grade 0 for all hydrophilic BL27 IOLs. There were no correlations between the glistenings and contrast sensitivity ($R=-0.25$, $P>0.05$), CDVA ($R=0.06$, $P>0.05$), or IOL power ($R=-0.0086$, $P=0.96$).

6.2.3 PCO

There were no significant differences in the CDVA between the groups ($P>0.05$). The median survival time without Nd:YAG capsulotomy was 2.6 years in the hydrophilic BL27 group and over 9 years in the hydrophobic AcrySof SA60AT IOL. The survival rates without Nd:YAG capsulotomy did not differ significantly regarding gender, operated eye, or patient age at surgery ($P>0.05$ for all comparisons).

Study III was an extended follow-up study at 9 years. Data from earlier follow-ups[69, 125] at 1 and 2 years postoperatively were retrieved to compare how the PCO developed. The results (table 1) show that values increased for both IOLs, but the hydrophilic IOL had an accelerated increase of Nd:YAG capsulotomies, PCO area, and PCO severity between 1 to 2 years postoperatively compared to the hydrophobic IOL.

Table 1. Summary of cumulative Nd:YAG capsulotomy rate, PCO area, and severity at the 1-, 2-, and 9-year follow-up visits.

Parameters	Cumulative Nd:YAG rate (%)		PCO area (%) (Median)		PCO severity (Median)	
Follow-up	AcrySof SA60AT IOL	BL27 IOL	AcrySof SA60AT IOL	BL27 IOL	AcrySof SA60AT IOL	BL27 IOL
1 year	5	3	4.65	18.2	0.055	0.18
2 year	10	40	4.5	46	0.045	0.74
9 year	28	67	13.4 (0-100)†	100 (49-100)†	0.26 (0-3)†	3 (1-3)†

†=range lower to upper quartile

6.3 STUDY IV

6.3.1 Patient data

Forty-three patients were included in this prospective randomized study, 21 in the standard-settings group and 22 in the low-settings group. Measurements performed 3 weeks and 3 months postoperatively in one patient in the standard-settings group were excluded from the calculations because the patient needed treatment with an oral nonsteroidal anti-inflammatory drug for another disease.

6.3.2 Fluidics and the impact on postoperative parameters

There were no significant differences between the groups regarding the postoperative parameters CDVA, CCT, anterior chamber flare, IOP, macular thickness, or ECD up to 3 months after phacoemulsification cataract surgery (P>0.05 for all comparisons). The surgical time was significantly longer (P<0.01) and the CDE was significantly higher (P<0.001) in the group with low fluidic settings. The median surgical time in the standard-settings group was 7 minutes and 20 seconds and 8 minutes and 28 seconds in the low-settings group. The mean CDE was 7.61 ± 3.61 (SD) in the standard-settings group and 15.14 ± 5.0 (SD) in the low-settings group.

7 DISCUSSION

7.1 STUDIES I-III

7.1.1 Lens glistenings

Different hydrophobic IOLs do not develop glistenings to the same extent as we showed that the AcrySof IOL did in study I. The hydrophobic AcrySof IOL developed much more glistenings as Tognetto et al.[7] reported earlier in a glistening study that evaluated AcrySof IOLs compared to another hydrophobic IOL. The investigators compared development of glistenings in seven different IOLs, two (AcrySof and Sensar) were hydrophobic acrylic IOLs. The AcrySof IOL showed a continuous increase in glistenings over 2 years and more glistenings than the Sensar IOL.

An in vitro study[12] that simulated 20-year deterioration of IOLs included six different hydrophobic acrylic IOLs, AcrySof MA60BM, AcrySof SA60AT, Sensar AR40e, Acryfold VA-60BB, Nex-Acri N4-18B, and Avansee AU6, showed that only the last IOL did not develop glistenings. The authors described the characteristics of glistening development in each IOLs, but they did not rank them.

Study II compared one hydrophobic IOL with a hydrophilic IOL 9 years postoperatively and showed that the hydrophilic IOL was not prone to glistening development even over the long term. This agreed with an earlier short-term follow-up study conducted for hydrophilic IOLs[7]. No other in vivo study of glistening development in hydrophilic IOLs has been conducted until now.

The severity of glistenings development in one in vitro study simulating accelerated 20-year IOL deterioration included a series of hydrophobic IOLs[12]. The tendency was that IOLs with higher water content developed fewer glistening-like opacities.

Another issue is the differences in refractive indices between the hydrophobic IOLs we studied, 1.55 for the AcrySof IOL and 1.47 for the Sensar AR40e IOL. Aqueous humor has a refractive index of 1.336, which is very close to that of water (1.333). When differences in refractive indices between two media (i.e., IOL material and water) increase, the amount of reflected light rays also increases according to Snell's law[126]. The higher refractive index in the AcrySof IOL compared to the refractive index of the Sensar IOL also may make glistenings more visible at the slit-lamp and in the Scheimpflug images.

To quantify glistenings in IOLs, we used Scheimpflug images in studies I and II. This method has been described earlier[23 29] and also was positively correlated with slit-lamp gradings[14]. Study I agreed with this study and found a correlation between quantified analyses of glistenings using Scheimpflug images with subjective slit-lamp grading of glistenings.

Surface light scattering and PCO are two potential sources of error when analyzing glistenings with Scheimpflug images, because these two phenomena also can be seen in the images as whitish bands of light scatterings in the IOL anterior and posterior surfaces. Eliminating these two phenomena from the calculations can be accomplished by omitting light scattering values from the IOL anterior and posterior surfaces, thus only light scatterings within the IOL (i.e., glistenings) are analyzed. We analyzed glistenings in the central parts of the IOL by subtracting light scattering from 73 microns and 101 microns from the IOL anterior and posterior surfaces and referred to them as deep and very deep glistenings, respectively. Excluding cases with PCO in the visual axis is another way to be certain to not include PCO in the calculations. Scheimpflug images appear to be a valuable and reliable tool and until now the only method to quantify glistenings objectively.

The CDVA and contrast sensitivity (studies I and II) were not correlated with the amount of glistenings as in most earlier studies[7 15 20 28 37 127 128]. The IOL dioptric power was not correlated with glistenings in studies I and II. The results from earlier studies are inconclusive; some show correlations with glistenings[13 15 17 20 129] and some do not[128 130].

A weakness of the studies was the large number of patient dropouts, i.e., 30% in study I and 35% in studies II and III. Long-term follow-up studies have this problem because patients become older and die, get ill, or move.

7.1.2 PCO

Long-term follow-up studies of PCO (studies I and III) are important because the average patient with an IOL is likely to have it for about 10 years, since the average age at surgery in many studies of patients with senile cataracts is 68 to 73 years. The average lifespan in Sweden was 83.7 years for women and 80.1 years for men in 2013 according to Statistics Sweden (Statistiska centralbyrån)[131], an authority in Sweden. We have seen cases in which the long-term follow-up of PCO development has yielded surprising results. One example was that the sharp posterior edge design in a hydrophobic acrylic IOL inhibits PCO more effectively for the first 3 to 5 years compared to a silicone IOL with a round-edge design[100]. After 12 years, the rates of PCO development and Nd:YAG in sharp-edge IOLs catch up with the round-edge IOLs[93]. Two other studies have reported similar results with loss of the advantageous PCO inhibitory features compared to silicone IOLs 6 years postoperatively[91 92].

In study I, we compared two hydrophobic acrylic IOLs with a sharp-edge design for PCO development. To our knowledge, this study had the longest follow-up time for comparing two different hydrophobic IOLs for PCO development. There were no significant differences in PCO area, severity, or Nd:YAG capsulotomy rates between the IOLs 5 to 7 years postoperatively and the study had results similar to other studies with shorter follow-up times[132-136].

In study III, we compared PCO development between a hydrophilic IOL (BL27) and a hydrophobic IOL (AcrySof SA60AT) 9 years postoperatively. This study had the longest follow-up time comparing PCO development between hydrophilic and hydrophobic acrylic IOLs. We concluded that the advantageous PCO inhibitory effect in the hydrophobic IOL at 2 year postoperatively remained valid even after 9 years. The superior PCO inhibitory characteristics of the hydrophobic acrylic IOL may depend on many different factors, i.e., the sharp-edge IOL profile and the stronger bindings of the AcrySof IOL to the posterior capsule. Strong binding of the posterior capsule to the posterior IOL surface minimizes any space for LECs to grow into the posterior capsule according to the concept of "no space, no cells"[48]. The hydrophobic AcrySof SA60AT IOL has these characteristics[43 74-76]. We mentioned previously that the sharp-edge hydrophilic IOLs generally are not as sharp as hydrophobic IOLs mostly due to different manufacturing techniques. The edge sharpness of BL27 IOL has not been studied earlier. It is then difficult to determine if the primary superior PCO inhibitory factor is the sharp-edge design or the strong fibronectin binding in our study. But earlier study[74] support the sharp-edge IOL profile as the most important factor inhibiting PCO development.

In study III, we also compared Nd:YAG capsulotomy rates between two different IOLs with survival analysis. Long-term follow-up studies usually have many patient dropouts and simply comparing Nd:YAG numbers becomes unreliable. The advantage in survival analysis is that all patient data are valuable and can be used up to the point at which they are lost to follow-up.

7.2 STUDY IV

The study results were interesting, because it was unexpected that lower fluidic settings did not have any substantial benefits compared to standard fluidic settings concerning postoperative parameters indicating surgical trauma. The disadvantages with low fluidic settings were a significantly longer surgical time and use of more CDE.

Few studies have been conducted in this field. Two earlier studies have investigated fluidic levels and the impact on the eye. Baradaran-Rafii et al.[108] compared low versus high aspiration parameters in longitudinal phacoemulsification. Their fluidic parameters were almost the same as ours, except that our vacuum levels were higher. Those investigators concluded that decreased ECD postoperatively was related to CDE. Increased CDE yielded decreased ECD. One important difference between our and their study was that we used torsional phacoemulsification, which is more effective than longitudinal phacoemulsification in lens aspiration[137-144], and it produces less heat[138 145] with less increase in postoperative corneal thickness[143 144] and less endothelial cell loss[143].

Vasavada et al[109] found a lower increase in CCT 1 and 7 days postoperatively with low fluidic settings compared with high fluidic settings. Those investigators had higher CDE for both fluidic settings groups compared to our study. They used the Infiniti Vision System as we did, but the difference was that they performed longitudinal phacoemulsification.

We cannot state to what extent torsional phacoemulsification plays a role and results in no significant differences in the postoperative parameters. Probably the duration of surgery, CDE amount, and fluidic levels are important factors. However, the purpose of our study was not to determine any threshold levels for tissue damage for the respective factors. More studies are needed in the future to establish these correlations. We can conclude that in normal daily cases with senile cataracts, there were no significant differences in the postoperative parameters between standard fluidic and low fluidic settings in phacoemulsification cataract surgery. The low fluidic settings were a bit disadvantageous because of the extended surgical time and the demand for a higher amount of ultrasound energy.

A weakness in this study was the small number of patients. With more patients, significant differences may be seen that we were unable to detect.

8 MAIN CONCLUSIONS

In study I, the AcrySof SA60AT IOL developed significantly more glistenings than the Sensar AR40e IOL, both hydrophobic acrylic IOLs, 5 to 7 years after phacoemulsification cataract surgery. Development of PCO area and severity and the frequency of Nd:YAG laser capsulotomy did not differ between the AcrySof SA60AT and Sensar AR40e IOLs 5 to 7 years postoperatively.

In study II, the AcrySof SA60AT IOL, a hydrophobic acrylic IOL, developed significantly more glistenings compared to the BL27 IOL, a hydrophilic acrylic IOL, 9 years after phacoemulsification cataract surgery.

In study III, the AcrySof SA60AT IOL had a significantly longer survival time without Nd:YAG laser capsulotomy compared to the BL27 IOL, 9 years after phacoemulsification cataract surgery.

In study IV, there were no significant differences in the postoperative parameters indicating surgical trauma between the standard and low fluidic settings in phacoemulsification cataract surgery. However, the surgical time was longer in the low-fluidic-settings group, and more phacoemulsification energy was needed to aspirate the lens.

9 FUTURE PERSPECTIVES

Thus far, glistenings have not been a big issue in relation to symptomatic complaints from patients who have undergone phacoemulsification cataract surgery. Is it necessary to further investigate this matter? In my opinion, it is certainly worth the effort, because according to the studies, glistenings may increase with time. The average lifespan has been increasing for many years in Sweden and worldwide, and the average patient age for IOL implantation during cataract surgery is slightly lower than before, i.e., 76 years in 1999 compared to 74 years in 2013 (Swedish National Cataract Registry annual report 2013)[146]. This means that the average patient is going to have their IOL for a longer period and the possibility for developing glistenings and PCO also increases.

In most cases, patients only undergo IOL implantation once because of the risk of complications when trying to explant the old IOL and re-implant a new IOL. Therefore, it is important that we implant the most satisfactory IOLs initially. That includes lowering the rates or if possible even eradicating glistenings and PCO to maximize the chances of the best postoperative outcomes.

In our studies, the average patient age was about 70 years. However, there is an increasing market for presbyopic refractive surgery due to the popularity and potential with gradually safer phacoemulsification machines, improved surgical techniques, and better IOL materials. These patients are often younger than most patients in the studies of glistenings and PCO and they are still in the workforce, tend to have better CDVA and contrast sensitivity preoperatively, and are more demanding of perfect results. If the contrast sensitivity decreases only slightly in this group, it may be enough to lead to visual symptoms and complaints. It is not rare that the implanted IOLs in these patients are premium IOLs with toric and multifocal characteristics. Performing Nd:YAG capsulotomy in patients with these lenses is best avoided if possible. Potential complications of Nd:YAG capsulotomy such as IOL dislocation and tilting with IOL decentration may cause more pronounced visual symptoms compared to monofocal IOLs.

Multifocal IOLs decrease contrast sensitivity by about 20% compared to standard monofocal IOLs[147-151]. Could this reduction in contrast sensitivity in a younger group of patients together with development of glistenings reach a threshold level at which visual symptoms occur and is this a new group of patients we should expect to see in the ophthalmology wards in a few years? I think it would be interesting to investigate the development of glistenings in premium IOLs and their impact on CDVA and contrast sensitivity.

Many different methods have been used to decrease the PCO rates. However, is it possible to eradicate it or further decrease PCO rates? Studies by Tassignon et al.[152 153], using the so-called bag-in-the-lens technique with a posterior capsulorhexis, have shown promising results, but creating a posterior capsulorhexis in the center and with almost the same diameter every time can be challenging. Could the new femtosecond laser surgical technique be helpful? Study of PCO development using the bag-in-the-lens technique with a femtosecond laser also may be worth considering, making an eventual second visit for Nd:YAG capsulotomy obsolete. With even better knowledge in these fields of research, we can provide feedback to the IOL and surgery machine manufacturers and they in turn can develop even better IOLs and machines and minimize intraoperative and postoperative complications.

There are new commercially available phacoemulsification machines that claim to control the anterior chamber depth and an IOP more stable than before. It would be interesting to study the fluidic settings and the impact on postoperative parameters when the IOP can be maintained at a stable and almost fix level throughout the entire surgery, allowing further study of different factors and their respective impact on the eye.

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11 REFERENCES

1. Ballin N. Glistenings in injection-molded lens. *J Am Intraocul Implant Soc* 1984;10(4):473.

2. Werner L. Glistenings and surface light scattering in intraocular lenses. *J Cataract Refract Surg* 2010;36(8):1398-420.

3. Miyata A, Yaguchi S. Equilibrium water content and glistenings in acrylic intraocular lenses. *J Cataract Refract Surg* 2004;30(8):1768-72.

4. Saylor DM, Coleman Richardson D, Dair BJ, Pollack SK. Osmotic cavitation of elastomeric intraocular lenses. *Acta Biomater* 2010;6(3):1090-8.

5. Shiba T, Mitooka K, Tsuneoka H. In vitro analysis of AcrySof intraocular lens glistening. *Eur J Ophthalmol* 2003;13(9-10):759-63.

6. Kato K, Nishida M, Yamane H, Nakamae K, Tagami Y, Tetsumoto K. Glistening formation in an AcrySof lens initiated by spinodal decomposition of the polymer network by temperature change. *J Cataract Refract Surg* 2001;27(9):1493-8.

7. Tognetto D, Toto L, Sanguinetti G, Ravalico G. Glistenings in foldable intraocular lenses. *J Cataract Refract Surg* 2002;28(7):1211-6.

8. Gregori NZ, Spencer TS, Mamalis N, Olson RJ. In vitro comparison of glistening formation among hydrophobic acrylic intraocular lenses(1). *J Cataract Refract Surg* 2002;28(7):1262-8.

9. Miura M, Osako M, Elsner AE, Kajizuka H, Yamada K, Usui M. Birefringence of intraocular lenses. *J Cataract Refract Surg* 2004;30(7):1549-55.

10. Miyata A, Uchida N, Nakajima K, Yaguchi S. Clinical and Experimental Observation of Glistening in Acrylic Intraocular Lenses. *Jpn J Ophthalmol* 2000;44(6):693.

11. Allers A, Baumeister M, Steinkamp GW, Ohrloff C, Kohnen T. [Intra-individual comparison of intraocular lenses of highly refractive silicone (Allergan SI40NB) and hydrophobic acrylate (Alcon Acrysof MA60BM). 1-year follow-up]. *Ophthalmologe* 2000;97(10):669-75.

12. Kawai K, Hayakawa K, Suzuki T. Simulation of 20-year deterioration of acrylic IOLs using severe accelerated deterioration tests. *Tokai J Exp Clin Med* 2012;37(3):62-5.

13. Ronbeck M, Behndig A, Taube M, Koivula A, Kugelberg M. Comparison of glistenings in intraocular lenses with three different materials: 12-year follow-up. *Acta Ophthalmol* 2013;91(1):66-70.

14. Behndig A, Monestam E. Quantification of glistenings in intraocular lenses using Scheimpflug photography. *J Cataract Refract Surg* 2009;35(1):14-7.

15. Moreno-Montanes J, Alvarez A, Rodriguez-Conde R, Fernandez-Hortelano A. Clinical factors related to the frequency and intensity of glistenings in AcrySof intraocular lenses. *J Cataract Refract Surg* 2003;29(10):1980-4.

16. Peetermans E, Hennekes R. Long-term results of wagon wheel packed acrylic intra-ocular lenses (AcrySof). *Bull Soc Belge Ophtalmol* 1999;271:45-8.

17. Monestam E, Behndig A. Impact on visual function from light scattering and glistenings in intraocular lenses, a long-term study. *Acta Ophthalmol* 2011;89(8):724-8.

18. Omar O, Pirayesh A, Mamalis N, Olson RJ. In vitro analysis of AcrySof intraocular lens glistenings in AcryPak and Wagon Wheel packaging. *J Cataract Refract Surg* 1998;24(1):107-13.

19. Nishihara H KT, Ohnishi T, Koike M, Imai M,, Shibuya A YS. [Glistenings in lathe-cut acrylic intraocular lens]. [Japanese]. *Ganka Shujutsu* 2000;13:227-30.

20. Colin J, Orignac I, Touboul D. Glistenings in a large series of hydrophobic acrylic intraocular lenses. *J Cataract Refract Surg* 2009;35(12):2121-6.

21. Dick HB, Olson RJ, Augustin AJ, Schwenn O, Magdowski G, Pfeiffer N. Vacuoles in the Acrysof intraocular lens as factor of the presence of serum in aqueous humor. *Ophthalmic Res* 2001;33(2):61-7.

22. Miyake K, Ota I, Maekubo K, Ichihashi S, Miyake S. Latanoprost accelerates disruption of the blood-aqueous barrier and the incidence of angiographic cystoid macular edema in early postoperative pseudophakias. *Arch Ophthalmol* 1999;117(1):34-40.

23. Ayaki M, Nishihara H, Yaguchi S, Koide R. Surfactant induced glistenings: surface active ingredients in ophthalmic solutions may enhance water entry into the voids of implanted acrylic intraocular lenses. *J Long Term Eff Med Implants* 2006;16(6):451-7.

24. Ayaki M, Nishihara H, Yaguchi S, Koide R. Effect of ophthalmic solution components on acrylic intraocular lenses. *J Cataract Refract Surg* 2007;33(1):122-6.

25. Dhaliwal DK, Mamalis N, Olson RJ, Crandall AS, Zimmerman P, Alldredge OC, et al. Visual significance of glistenings seen in the AcrySof intraocular lens. *J Cataract Refract Surg* 1996;22(4):452-7.

26. Cisneros-Lanuza A, Hurtado-Sarrio M, Duch-Samper A, Gallego-Pinazo R, Menezo-Rozalen JL. Glistenings in the Artiflex phakic intraocular lens. *J Cataract Refract Surg* 2007;33(8):1405-8.

27. Gunenc U, Oner FH, Tongal S, Ferliel M. Effects on visual function of glistenings and folding marks in AcrySof intraocular lenses. *J Cataract Refract Surg* 2001;27(10):1611-4.

28. Chang A, Behndig A, Ronbeck M, Kugelberg M. Comparison of posterior capsule opacification and glistenings with 2 hydrophobic acrylic intraocular lenses: 5- to 7-year follow-up. *J Cataract Refract Surg* 2013;39(5):694-8.

29. Klos KM, Richter R, Schnaudigel O, Ohrloff C. Image analysis of implanted rigid and foldable intraocular lenses in human eyes using Scheimpflug photography. *Ophthalmic Res* 1999;31(2):130-3.

30. Nishihara H, Ayaki M, Watanabe T, Ohnishi T, Kageyama T, Yaguchi S. [Comparison of surface light scattering of acrylic intraocular lenses made by lathe-cutting and cast-molding methods--long-term observation and experimental study]. *Nihon Ganka Gakkai Zasshi* 2004;108(3):157-61.

31. Yaguchi S, Chida M, Nishihara H, Ohnishi T, Ayaki M. [Light scattering observed on the surface of acrylic intraocular lenses ten years after implantation]. *Nihon Ganka Gakkai Zasshi* 2002;106(2):109-11.

32. Wilkins E, Olson RJ. Glistenings with long-term follow-up of the Surgidev B20/20 polymethylmethacrylate intraocular lens. *Am J Ophthalmol* 2001;132(5):783-5.

33. Packer M, Fry L, Lavery KT, Lehmann R, McDonald J, Nichamin L, et al. Safety and effectiveness of a glistening-free single-piece hydrophobic acrylic intraocular lens (enVista). *Clin Ophthalmol* 2013;7:1905-12.

34. Packer M, Rajan M, Ligabue E, Heiner P. Clinical properties of a novel, glistening-free, single-piece, hydrophobic acrylic IOL. *Clin Ophthalmol* 2014;8:421-7.

35. Tetz MR WL, Schwahn-Bendig S, Batlle JF. Prospective clinical study to quantify glistenings in new hydrophobic acrylic IOL. *Paper presented at the ASCRS Symposium on Cataract, IOL and Refractive Surgery*. San Francisco, CA, April 2009, 2009.

36. Hayashi K, Hirata A, Yoshida M, Yoshimura K, Hayashi H. Long-term effect of surface light scattering and glistenings of intraocular lenses on visual function. *Am J Ophthalmol* 2012;154(2):240-51 e2.

37. Chang A, Kugelberg M. Glistenings 9 years after phacoemulsification in hydrophobic and hydrophilic acrylic intraocular lenses. *J Cataract Refract Surg* 2015;41(6):1199-204.

38. Waite A, Faulkner N, Olson RJ. Glistenings in the single-piece, hydrophobic, acrylic intraocular lenses. *Am J Ophthalmol* 2007;144(1):143-4.

39. Apple DJ, Peng Q, Visessook N, Werner L, Pandey SK, Escobar-Gomez M, et al. Eradication of posterior capsule opacification: documentation of a marked decrease in Nd:YAG laser posterior capsulotomy rates noted in an analysis of 5416 pseudophakic human eyes obtained postmortem. *Ophthalmology* 2001;108(3):505-18.

40. Apple DJ, Peng Q, Visessook N, Werner L, Pandey SK, Escobar-Gomez M, et al. Surgical prevention of posterior capsule opacification. Part 1: Progress in eliminating this complication of cataract surgery. *Journal of cataract and refractive surgery* 2000;26(2):180-7.

41. Thompson AM, Sachdev N, Wong T, Riley AF, Grupcheva CN, McGhee CN. The Auckland Cataract Study: 2 year postoperative assessment of aspects of clinical, visual, corneal topographic and satisfaction outcomes. *Br J Ophthalmol* 2004;88(8):1042-8.

42. Smith SR, Daynes T, Hinckley M, Wallin TR, Olson RJ. The effect of lens edge design versus anterior capsule overlap on posterior capsule opacification. *Am J Ophthalmol* 2004;138(4):521-6.

43. Meacock WR, Spalton DJ, Hollick EJ, Barman S, Boyce JF. The effect of polymethylmethacrylate and acrysof intraocular lenses on the posterior capsule in patients with a large capsulorrhexis. *Jpn J Ophthalmol* 2001;45(4):348-54.

44. Wejde G, Kugelberg M, Zetterstrom C. Position of anterior capsulorhexis and posterior capsule opacification. *Acta Ophthalmol Scand* 2004;82(5):531-4.

45. Mamalis N, Grossniklaus HE, Waring GO, 3rd, Werner L, Brubaker J, Davis D, et al. Ablation of lens epithelial cells with a laser photolysis system: histopathology, ultrastructure, and immunochemistry. *J Cataract Refract Surg* 2010;36(6):1003-10.

46. Meacock WR, Spalton DJ, Hollick EJ, Boyce JF, Barman S, Sanguinetti G. Double-masked prospective ocular safety study of a lens epithelial cell antibody to prevent posterior capsule opacification. *J Cataract Refract Surg* 2000;26(5):716-21.

47. Fernandez V, Fragoso MA, Billotte C, Lamar P, Orozco MA, Dubovy S, et al. Efficacy of various drugs in the prevention of posterior capsule opacification: experimental study of rabbit eyes. *J Cataract Refract Surg* 2004;30(12):2598-605.

48. Apple DJ, Solomon KD, Tetz MR, Assia EI, Holland EY, Legler UF, et al. Posterior capsule opacification. *Surv Ophthalmol* 1992;37(2):73-116.

49. Koch DD, Liu JF, Gill EP, Parke DW, 2nd. Axial myopia increases the risk of retinal complications after neodymium-YAG laser posterior capsulotomy. *Arch Ophthalmol* 1989;107(7):986-90.

50. Burq MA, Taqui AM. Frequency of retinal detachment and other complications after neodymium:Yag laser capsulotomy. *J Pak Med Assoc* 2008;58(10):550-2.

51. Ari S, Cingu AK, Sahin A, Cinar Y, Caca I. The effects of Nd:YAG laser posterior capsulotomy on macular thickness, intraocular pressure, and visual acuity. *Ophthalmic Surg Lasers Imaging* 2012;43(5):395-400.

52. Holweger RR, Marefat B. Intraocular pressure change after neodymium:YAG capsulotomy. *J Cataract Refract Surg* 1997;23(1):115-21.

53. Buehl W, Findl O. Effect of intraocular lens design on posterior capsule opacification. *J Cataract Refract Surg* 2008;34(11):1976-85.

54. Newland TJ, McDermott ML, Eliott D, Hazlett LD, Apple DJ, Lambert RJ, et al. Experimental neodymium:YAG laser damage to acrylic, poly(methyl methacrylate), and silicone intraocular lens materials. *J Cataract Refract Surg* 1999;25(1):72-6.

55. Charles S. Vitreoretinal complications of YAG laser capsulotomy. *Ophthalmol Clin North Am* 2001;14(4):705-10.

56. Meacock WR, Spalton DJ, Boyce J, Marshall J. The effect of posterior capsule opacification on visual function. *Invest Ophthalmol Vis Sci* 2003;44(11):4665-9.

57. Jose RM, Bender LE, Boyce JF, Heatley C. Correlation between the measurement of posterior capsule opacification severity and visual function testing. *J Cataract Refract Surg* 2005;31(3):534-42.

58. Cheng CY, Yen MY, Chen SJ, Kao SC, Hsu WM, Liu JH. Visual acuity and contrast sensitivity in different types of posterior capsule opacification. *J Cataract Refract Surg* 2001;27(7):1055-60.

59. Guha GS. Soemmering's ring and its dislocations. *Br J Ophthalmol* 1951;35(4):226-31.

60. Dana MR, Chatzistefanou K, Schaumberg DA, Foster CS. Posterior capsule opacification after cataract surgery in patients with uveitis. *Ophthalmology* 1997;104(9):1387-93; discussion 93-4.

61. Ebihara Y, Kato S, Oshika T, Yoshizaki M, Sugita G. Posterior capsule opacification after cataract surgery in patients with diabetes mellitus. *J Cataract Refract Surg* 2006;32(7):1184-7.

62. Hayashi K, Hayashi H, Nakao F, Hayashi F. Posterior capsule opacification after cataract surgery in patients with diabetes mellitus. *Am J Ophthalmol* 2002;134(1):10-6.

63. Hayashi Y, Kato S, Fukushima H, Numaga J, Kaiya T, Tamaki Y, et al. Relationship between anterior capsule contraction and posterior capsule opacification after cataract surgery in patients with diabetes mellitus. *J Cataract Refract Surg* 2004;30(7):1517-20.

64. Praveen MR, Vasavada AR, Shah GD, Shah AR, Khamar BM, Dave KH. A prospective evaluation of posterior capsule opacification in eyes with diabetes mellitus: a case-control study. *Eye (Lond)* 2014;28(6):720-7.

65. Zaczek A, Zetterstrom C. Posterior capsule opacification after phacoemulsification in patients with diabetes mellitus. *J Cataract Refract Surg* 1999;25(2):233-7.

66. Dikopf MS, Chow CC, Mieler WF, Tu EY. Cataract extraction outcomes and the prevalence of zonular insufficiency in retinitis pigmentosa. *Am J Ophthalmol* 2013;156(1):82-88 e2.

67. Peng Q, Apple DJ, Visessook N, Werner L, Pandey SK, Escobar-Gomez M, et al. Surgical prevention of posterior capsule opacification. Part 2: Enhancement of cortical cleanup by focusing on hydrodissection. *J Cataract Refract Surg* 2000;26(2):188-97.

68. Heatley CJ, Spalton DJ, Kumar A, Jose R, Boyce J, Bender LE. Comparison of posterior capsule opacification rates between hydrophilic and hydrophobic single-piece acrylic intraocular lenses. *J Cataract Refract Surg* 2005;31(4):718-24.

69. Kugelberg M, Wejde G, Jayaram H, Zetterstrom C. Two-year follow-up of posterior capsule opacification after implantation of a hydrophilic or hydrophobic acrylic intraocular lens. *Acta Ophthalmol* 2008;86(5):533-6.

70. Ursell PG, Spalton DJ, Pande MV, Hollick EJ, Barman S, Boyce J, et al. Relationship between intraocular lens biomaterials and posterior capsule opacification. *J Cataract Refract Surg* 1998;24(3):352-60.

71. Hollick EJ, Spalton DJ, Ursell PG, Pande MV. Lens epithelial cell regression on the posterior capsule with different intraocular lens materials. *Br J Ophthalmol* 1998;82(10):1182-8.

72. Fong CS, Mitchell P, Rochtchina E, Cugati S, Hong T, Wang JJ. Three-year incidence and factors associated with posterior capsule opacification after cataract surgery: The Australian Prospective Cataract Surgery and Age-related Macular Degeneration Study. *Am J Ophthalmol* 2014;157(1):171-79 e1.

73. Nishi O, Nishi K. Preventing posterior capsule opacification by creating a discontinuous sharp bend in the capsule. *Journal of cataract and refractive surgery* 1999;25(4):521-6.

74. Nishi O, Nishi K, Akura J, Nagata T. Effect of round-edged acrylic intraocular lenses on preventing posterior capsule opacification. *J Cataract Refract Surg* 2001;27(4):608-13.

75. Nishi O, Nishi K, Sakanishi K. Inhibition of migrating lens epithelial cells at the capsular bend created by the rectangular optic edge of a posterior chamber intraocular lens. *Ophthalmic Surg Lasers* 1998;29(7):587-94.

76. Nishi O, Nishi K, Wickstrom K. Preventing lens epithelial cell migration using intraocular lenses with sharp rectangular edges. *Journal of cataract and refractive surgery* 2000;26(10):1543-9.

77. DW S. Beobachtungen über die organischen Veränderungen an Auge mit Staaroperationen. Frankfurt/Main: Wesche, 1828.

78. Werner L, Mamalis N, Pandey SK, Izak AM, Nilson CD, Davis BL, et al. Posterior capsule opacification in rabbit eyes implanted with hydrophilic acrylic intraocular lenses with enhanced square edge. *J Cataract Refract Surg* 2004;30(11):2403-9.

79. Buehl W, Findl O, Menapace R, Sacu S, Kriechbaum K, Koeppl C, et al. Long-term effect of optic edge design in an acrylic intraocular lens on posterior capsule opacification. *Journal of cataract and refractive surgery* 2005;31(5):954-61.

80. Findl O, Menapace R, Sacu S, Buehl W, Rainer G. Effect of optic material on posterior capsule opacification in intraocular lenses with sharp-edge optics: randomized clinical trial. *Ophthalmology* 2005;112(1):67-72.

81. Nanavaty MA, Spalton DJ, Boyce J, Brain A, Marshall J. Edge profile of commercially available square-edged intraocular lenses. *Journal of cataract and refractive surgery* 2008;34(4):677-86.

82. Sacu S, Menapace R, Findl O, Kiss B, Buehl W, Georgopoulos M. Long-term efficacy of adding a sharp posterior optic edge to a three-piece silicone intraocular lens on capsule opacification: five-year results of a randomized study. *American journal of ophthalmology* 2005;139(4):696-703.

83. Hayashi K, Hayashi H. Posterior capsule opacification in the presence of an intraocular lens with a sharp versus rounded optic edge. *Ophthalmology* 2005;112(9):1550-6.

84. Shah A, Spalton DJ, Gilbert C, Vasavada A, Boyce JF, Minassian D, et al. Effect of intraocular lens edge profile on posterior capsule opacification after extracapsular cataract surgery in a developing country. *J Cataract Refract Surg* 2007;33(7):1259-66.

85. Spalton D. Posterior capsule opacification: have we made a difference? *Br J Ophthalmol* 2013;97(1):1-2.

86. Hancox J, Spalton D, Cleary G, Boyce J, Nanavaty MA, Thyagarajan S, et al. Fellow-eye comparison of posterior capsule opacification with AcrySof SN60AT and AF-1 YA-60BB blue-blocking intraocular lenses. *Journal of cataract and refractive surgery* 2008;34(9):1489-94.

87. Li Y, Wang J, Chen Z, Tang X. Effect of hydrophobic acrylic versus hydrophilic acrylic intraocular lens on posterior capsule opacification: meta-analysis. *PLoS One* 2013;8(11):e77864.

88. Vasavada AR, Raj SM, Shah A, Shah G, Vasavada V. Comparison of posterior capsule opacification with hydrophobic acrylic and hydrophilic acrylic intraocular lenses. *J Cataract Refract Surg* 2011;37(6):1050-9.

89. Linnola RJ, Werner L, Pandey SK, Escobar-Gomez M, Znoiko SL, Apple DJ. Adhesion of fibronectin, vitronectin, laminin, and collagen type IV to intraocular lens materials in pseudophakic human autopsy eyes. Part 1: histological sections. *Journal of cataract and refractive surgery* 2000;26(12):1792-806.

90. Linnola RJ, Werner L, Pandey SK, Escobar-Gomez M, Znoiko SL, Apple DJ. Adhesion of fibronectin, vitronectin, laminin, and collagen type IV to intraocular lens materials in pseudophakic human autopsy eyes. Part 2: explanted intraocular lenses. *Journal of cataract and refractive surgery* 2000;26(12):1807-18.

91. Vock L, Crnej A, Findl O, Neumayer T, Buehl W, Sacu S, et al. Posterior capsule opacification in silicone and hydrophobic acrylic intraocular lenses with sharp-edge optics six years after surgery. *Am J Ophthalmol* 2009;147(4):683-90 e2.

92. Vock L, Menapace R, Stifter E, Georgopoulos M, Sacu S, Buhl W. Posterior capsule opacification and neodymium:YAG laser capsulotomy rates with a round-edged silicone and a sharp-edged hydrophobic acrylic intraocular lens 10 years after surgery. *J Cataract Refract Surg* 2009;35(3):459-65.

93. Ronbeck M, Kugelberg M. Posterior capsule opacification with 3 intraocular lenses: 12-year prospective study. *J Cataract Refract Surg* 2014;40(1):70-6.

94. Barman SA, Hollick EJ, Boyce JF, Spalton DJ, Uyyanonvara B, Sanguinetti G, et al. Quantification of posterior capsular opacification in digital images after cataract surgery. *Invest Ophthalmol Vis Sci* 2000;41(12):3882-92.

95. Bender L, Spalton DJ, Uyanonvara B, Boyce J, Heatley C, Jose R, et al. POCOman: new system for quantifying posterior capsule opacification. *J Cataract Refract Surg* 2004;30(10):2058-63.

96. Findl O, Buehl W, Menapace R, Georgopoulos M, Rainer G, Siegl H, et al. Comparison of 4 methods for quantifying posterior capsule opacification. *J Cataract Refract Surg* 2003;29(1):106-11.

97. Hayashi K, Hayashi H, Nakao F, Hayashi F. Correlation between posterior capsule opacification and visual function before and after Neodymium: YAG laser posterior capsulotomy. *Am J Ophthalmol* 2003;136(4):720-6.

98. Hayashi H, Hayashi K, Nakao F, Hayashi F. Quantitative comparison of posterior capsule opacification after polymethylmethacrylate, silicone, and soft acrylic intraocular lens implantation. *Arch Ophthalmol* 1998;116(12):1579-82.

99. Buehl W, Findl O, Menapace R, Sacu S, Kriechbaum K, Koeppl C, et al. Long-term effect of optic edge design in an acrylic intraocular lens on posterior capsule opacification. *J Cataract Refract Surg* 2005;31(5):954-61.

100. Ronbeck M, Zetterstrom C, Wejde G, Kugelberg M. Comparison of posterior capsule opacification development with 3 intraocular lens types: five-year prospective study. *J Cataract Refract Surg* 2009;35(11):1935-40.

101. Wejde G, Kugelberg M, Zetterstrom C. Posterior capsule opacification: comparison of 3 intraocular lenses of different materials and design. *J Cataract Refract Surg* 2003;29(8):1556-9.

102. Kelman CD. Phaco-emulsification and aspiration. A new technique of cataract removal. A preliminary report. *Am J Ophthalmol* 1967;64(1):23-35.

103. Kohnen T, Baumeister M, Kook D, Klaproth OK, Ohrloff C. Cataract surgery with implantation of an artificial lens. *Dtsch Arztebl Int* 2009;106(43):695-702.

104. de Silva SR, Riaz Y, Evans JR. Phacoemulsification with posterior chamber intraocular lens versus extracapsular cataract extraction (ECCE) with posterior chamber intraocular lens for age-related cataract. *Cochrane Database Syst Rev* 2014;1:CD008812.

105. Riaz Y, Mehta JS, Wormald R, Evans JR, Foster A, Ravilla T, et al. Surgical interventions for age-related cataract. *Cochrane Database Syst Rev* 2006(4):CD001323.

106. Chee SP, Ti SE, Sivakumar M, Tan DT. Postoperative inflammation: extracapsular cataract extraction versus phacoemulsification. *J Cataract Refract Surg* 1999;25(9):1280-5.

107. Pande MV, Spalton DJ, Kerr-Muir MG, Marshall J. Postoperative inflammatory response to phacoemulsification and extracapsular cataract surgery: aqueous flare and cells. *J Cataract Refract Surg* 1996;22 Suppl 1:770-4.

108. Baradaran-Rafii A, Rahmati-Kamel M, Eslani M, Kiavash V, Karimian F. Effect of hydrodynamic parameters on corneal endothelial cell loss after phacoemulsification. *J Cataract Refract Surg* 2009;35(4):732-7.

109. Vasavada AR, Praveen MR, Vasavada VA, Raj SM, Asnani PK, Garg VS. Impact of high and low aspiration parameters on postoperative outcomes of phacoemulsification: randomized clinical trial. *J Cataract Refract Surg* 2010;36(4):588-93.

110. Lundberg B, Jonsson M, Behndig A. Postoperative corneal swelling correlates strongly to corneal endothelial cell loss after phacoemulsification cataract surgery. *Am J Ophthalmol* 2005;139(6):1035-41.

111. Shah SM, Spalton DJ. Changes in anterior chamber flare and cells following cataract surgery. *Br J Ophthalmol* 1994;78(2):91-4.

112. Miyake K, Asakura M, Maekubo K. Consensual reactions of human blood-aqueous barrier to implant operations. *Arch Ophthalmol* 1984;102(4):558-61.

113. Ferguson VM, Spalton DJ. Recovery of the blood-aqueous barrier after cataract surgery. *Br J Ophthalmol* 1991;75(2):106-10.

114. Ferguson VM, Spalton DJ. Continued breakdown of the blood aqueous barrier following cataract surgery. *Br J Ophthalmol* 1992;76(8):453-6.

115. Ersoy L, Caramoy A, Ristau T, Kirchhof B, Fauser S. Aqueous flare is increased in patients with clinically significant cystoid macular oedema after cataract surgery. *Br J Ophthalmol* 2013;97(7):862-5.

116. Ursell PG, Spalton DJ, Whitcup SM, Nussenblatt RB. Cystoid macular edema after phacoemulsification: relationship to blood-aqueous barrier damage and visual acuity. *J Cataract Refract Surg* 1999;25(11):1492-7.

117. Bechmann M, Thiel MJ, Neubauer AS, Ullrich S, Ludwig K, Kenyon KR, et al. Central corneal thickness measurement with a retinal optical coherence tomography device versus standard ultrasonic pachymetry. *Cornea* 2001;20(1):50-4.

118. Airiani S, Trokel SL, Lee SM, Braunstein RE. Evaluating central corneal thickness measurements with noncontact optical low-coherence reflectometry and contact ultrasound pachymetry. *Am J Ophthalmol* 2006;142(1):164-5.

119. Kuerten D, Plange N, Koch EC, Koutsonas A, Walter P, Fuest M. Central corneal thickness determination in corneal edema using ultrasound pachymetry, a Scheimpflug camera, and anterior segment OCT. *Graefes Arch Clin Exp Ophthalmol* 2015;253(7):1105-9.

120. Hee MR, Puliafito CA, Wong C, Duker JS, Reichel E, Rutledge B, et al. Quantitative assessment of macular edema with optical coherence tomography. *Arch Ophthalmol* 1995;113(8):1019-29.

121. Mustonen RK, McDonald MB, Srivannaboon S, Tan AL, Doubrava MW, Kim CK. Normal human corneal cell populations evaluated by in vivo scanning slit confocal microscopy. *Cornea* 1998;17(5):485-92.

122. Bigar F, Herbort CP, Pittet N. [Tyndallometry of the anterior chamber with the Kowa FC-100 Laser FLare-Cell Meter]. *Klin Monbl Augenheilkd* 1991;198(5):396-8.

123. Shah SM, Spalton DJ, Taylor JC. Correlations between laser flare measurements and anterior chamber protein concentrations. *Invest Ophthalmol Vis Sci* 1992;33(10):2878-84.

124. Rydberg A, Han Y, Lennerstrand G. A comparison between different contrast sensitivity tests in the detection of amblyopia. *Strabismus* 1997;5(4):167-84.

125. Kugelberg M, Wejde G, Jayaram H, Zetterstrom C. Posterior capsule opacification after implantation of a hydrophilic or a hydrophobic acrylic intraocular lens: one-year follow-up. *J Cataract Refract Surg* 2006;32(10):1627-31.

126. Fishman RS. Perish, then publish: Thomas Harriot and the sine law of refraction. *Arch Ophthalmol* 2000;118(3):405-9.

127. Monestam E, Behndig A. Impact on visual function from light scattering and glistenings in intraocular lenses, a long-term study. *Acta Ophthalmol* 2010.

128. Colin J, Orignac I. Glistenings on intraocular lenses in healthy eyes: effects and associations. *J Refract Surg* 2011;27(12):869-75.

129. Colin J, Praud D, Touboul D, Schweitzer C. Incidence of glistenings with the latest generation of yellow-tinted hydrophobic acrylic intraocular lenses. *J Cataract Refract Surg* 2012;38(7):1140-6.

130. Xi L, Liu Y, Zhao F, Chen C, Cheng B. Analysis of glistenings in hydrophobic acrylic intraocular lenses on visual performance. *Int J Ophthalmol* 2014;7(3):446-51.

131. Statistiska C. Ettårig livslängdstabell för hela riket efter kön och ålder. År 2002 - 2014 2015.

132. Cullin F, Busch T, Lundstrom M. Economic considerations related to choice of intraocular lens (IOL) and posterior capsule opacification frequency - a comparison of three different IOLs. *Acta Ophthalmol* 2014;92(2):179-83.

133. Hayashi K, Yoshida M, Hayashi H. Comparison of posterior capsule opacification between fellow eyes with two types of acrylic intraocular lens. *Eye (Lond)* 2008;22(1):35-41.

134. Krall EM, Arlt EM, Jell G, Strohmaier C, Moussa S, Dexl AK. Prospective Randomized Intraindividual Comparison of Posterior Capsule Opacification After Implantation of an IOL With and Without Heparin Surface Modification. *J Refract Surg* 2015;31(7):466-72.

135. Nanavaty MA, Spalton DJ, Gala KB, Dhital A, Boyce J. Effect of intraocular lens asphericity on posterior capsule opacification between two intraocular lenses with same acrylic material: a fellow-eye study. *Acta Ophthalmol* 2012;90(2):e104-8.

136. Zemaitiene R, Jasinskas V. Prevention of posterior capsule opacification with 3 intraocular lens models: a prospective, randomized, long-term clinical trial. *Medicina (Kaunas)* 2011;47(11):595-9.

137. Davison JA. Cumulative tip travel and implied followability of longitudinal and torsional phacoemulsification. *J Cataract Refract Surg* 2008;34(6):986-90.

138. Han YK, Miller KM. Heat production: Longitudinal versus torsional phacoemulsification. *J Cataract Refract Surg* 2009;35(10):1799-805.

139. Rekas M, Montes-Mico R, Krix-Jachym K, Klus A, Stankiewicz A, Ferrer-Blasco T. Comparison of torsional and longitudinal modes using phacoemulsification parameters. *J Cataract Refract Surg* 2009;35(10):1719-24.

140. El-Moatassem Kotb AM, Gamil MM. Torsional mode phacoemulsification: effective, safe cataract surgery technique of the future. *Middle East Afr J Ophthalmol* 2010;17(1):69-73.

141. Kim DH, Wee WR, Lee JH, Kim MK. The comparison between torsional and conventional mode phacoemulsification in moderate and hard cataracts. *Korean J Ophthalmol* 2010;24(6):336-40.

142. Miyoshi T, Yoshida H. Emulsification action of longitudinal and torsional ultrasound tips and the effect on treatment of the nucleus during phacoemulsification. *J Cataract Refract Surg* 2010;36(7):1201-6.

143. Vasavada AR, Raj SM, Patel U, Vasavada V. Comparison of torsional and microburst longitudinal phacoemulsification: a prospective, randomized, masked clinical trial. *Ophthalmic Surg Lasers Imaging* 2010;41(1):109-14.

144. Christakis PG, Braga-Mele RM. Intraoperative performance and postoperative outcome comparison of longitudinal, torsional, and transversal phacoemulsification machines. *J Cataract Refract Surg* 2012;38(2):234-41.

145. Jun B, Berdahl JP, Kim T. Thermal study of longitudinal and torsional ultrasound phacoemulsification: tracking the temperature of the corneal surface, incision, and handpiece. *J Cataract Refract Surg* 2010;36(5):832-7.

146. Zetterstrom C, Lundström M, Serring I, Montan P, Behndig A, Kugelberg M. Svensk Kataraktkirurgi Årsrapport 2013 baserad på data från Nationella Kataraktregistret. 2014.

147. Blaylock JF, Si Z, Aitchison S, Prescott C. Visual function and change in quality of life after bilateral refractive lens exchange with the ReSTOR multifocal intraocular lens. *J Refract Surg* 2008;24(3):265-73.

148. Sen HN, Sarikkola AU, Uusitalo RJ, Laatikainen L. Quality of vision after AMO Array multifocal intraocular lens implantation. *J Cataract Refract Surg* 2004;30(12):2483-93.

149. Kaushik S, Kamlesh. A clinical evaluation of an aspheric multifocal intraocular lens and its implications for the developing world. *Ophthalmic Surg Lasers* 2002;33(4):298-303.

150. Steinert RF, Post CT, Jr., Brint SF, Fritch CD, Hall DL, Wilder LW, et al. A prospective, randomized, double-masked comparison of a zonal-progressive multifocal intraocular lens and a monofocal intraocular lens. *Ophthalmology* 1992;99(6):853-60; discussion 60-1.

151. Post CT, Jr. Comparison of depth of focus and low-contrast acuities for monofocal versus multifocal intraocular lens patients at 1 year. *Ophthalmology* 1992;99(11):1658-63; discussion 63-4.

152. Tassignon MJ, De Groot V, Vrensen GF. Bag-in-the-lens implantation of intraocular lenses. *J Cataract Refract Surg* 2002;28(7):1182-8.

153. Tassignon MJ, De Veuster I, Godts D, Kosec D, Van den Dooren K, Gobin L. Bag-in-the-lens intraocular lens implantation in the pediatric eye. *J Cataract Refract Surg* 2007;33(4):611-7.